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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/775,879	02/02/2001	Sunghwa Choe	2225-0003	3956

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EXAMINER
BAUM, STUART F

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/775,879	CHOE ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *57-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with application* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

RCE Acknowledgment

1. The request filed on May 5, 2003 in paper no. 19 for a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114, based on parent Application No. 09/775879 is acceptable and a RCE has been established. An action on the RCE follows.

Claims 57-78 are pending.

Claims 1-56 have been canceled.

2. Claims 57-78 are examined in the present office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 57-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Rejection includes dependent claims.

In claims 57 and 73, the recitation "truncated N-terminal to a histidine cluster domain" is unclear as to how it relates to the rest of the sentence. Does Applicant mean that the truncation occurs in the N-terminal region of the polypeptide before the first histidine cluster domain?

In claims 62, 70, and 75 insert the word --transcriptional-- before the word "control".

In claim 65, 2nd line, insert --is located-- after the second "mutation".

In claim 68, 2nd line, insert --at a position-- after the word "and".

In claim 73, 4th line, insert --is-- after the word "desaturase".

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 57-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The inventors claim an isolated nucleic acid, or coding sequence that encodes a mutant delta-7 sterol C-5 desaturase polypeptide wherein said mutant delta-7 sterol C-5 desaturase is truncated in the N-terminal region of the polypeptide, N-terminal to a histidine cluster domain, or wherein the truncation occurs at a position N-terminal to the His1 or His3 histidine cluster domains, or wherein the truncation occurs at a position C-terminal to the His2 and N-terminal to the His3 histidine cluster domain, or wherein the isolated nucleic acid comprises a polynucleotide consisting of positions 143 to 322 or 143 to 1552 of SEQ ID NO:20 or a polynucleotide having 70% identity to one of the previous two sequences, and host cell and transgenic plant transformed therewith, or a method of producing a transgenic plant comprising introducing a polynucleotide of claim 57 operably linked to a transcription control element.

The Applicants originally identified the monogenic recessive *dwf7-1* mutant from a screen of 14,000 T-DNA transformed lines of *Arabidopsis*. The characteristic *dwf7-1*

phenotype includes, short robust stems, reduced fertility and dark-green, round and curled leaves. The *dwf7-1* mutation was found to be allelic to the *ste1* mutant which was previously shown to encode a delta 7 sterol C-5 desaturase.

The Applicants do not identify structural features unique to the *Arabidopsis dwf7* mutant protein, the functional domains of the protein or regions of the protein that when mutaganized produce a mutant protein. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Given the lack of description, one skilled in the art would not be able to identify sequences with less than 100% sequence identity to SEQ ID NO:20. The claims recite sequences that have a mutation in regions N-terminal or C-terminal to different histidine cluster domains or sequences that exhibit 70% sequence identity to regions of SEQ ID NO:20, but Applicants have not disclosed a representative number of species as encompassed by the claims. The claims encompass mutants and allelic variants and thus imply that structural variants exist in nature, yet only 2 structural variants have been disclosed. The implication is that there is a gene and a protein other than that disclosed which exists in nature, but the structure thereof is not known. Thus, there is insufficient relevant identifying characteristics to allow one skilled in the art to predictably determine such mutants and allelic variants from other plants and organisms, absent further

guidance. Therefore, the written description requirement is not satisfied. Therefore, one skilled in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention. (see Written Description Requirement published in Federal Register/Vol.66, No. 4/ Friday, January 5, 2001/Notices; p. 1099-1111).

Enablement

5. Claims 57-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn to an isolated nucleic acid, or coding sequence that encodes a mutant delta-7 sterol C-5 desaturase polypeptide wherein said mutant delta-7 sterol C-5 desaturase is truncated in the N-terminal region of the polypeptide, N-terminal to a histidine cluster domain, or wherein the truncation occurs at a position N-terminal to the His1 or His3 histidine cluster domains, or wherein the truncation occurs at a position C-terminal to the His2 and N-terminal to the His3 histidine cluster domain, or wherein the isolated nucleic acid comprises a polynucleotide consisting of positions 143 to 322 or 143 to 1552 of SEQ ID NO:20 or a polynucleotide having 70% identity to one of the previous two sequences, and host cell and transgenic plant transformed therewith, or a method of producing a transgenic plant comprising introducing a polynucleotide of claim 57 operably linked to a transcription control element.

The claimed invention is not supported by an enabling disclosure taking into account the *In re Wands* factors (858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number

of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The Applicants originally identified the monogenic recessive *dwf7-1* mutant from a screen of 14,000 T-DNA transformed lines of *Arabidopsis*. The characteristic *dwf7-1* phenotype includes, short robust stems, reduced fertility and dark-green, round and curled leaves. The *dwf7-1* mutation was found to be allelic to the *ste1* mutant which was previously shown to encode a delta 7 sterol C-5 desaturase.

The Applicants have not reduced to practice their invention. They have only described the cloning and characterization of the nucleic acid sequence. In particular, it has not been taught how transforming a plant with an above mentioned sequence will produce a dominant phenotype, or produce a plant with increased levels of episterol when compared to plants not transformed with Applicant's invention. It has not been taught how transforming a plant with the before mentioned sequences will over-ride or knockout the wild-type allele.

It cannot be predicted by one of skill in the art that nucleic acids that have 70% identity to bases 143 to 322 or bases 143 to 1552 of SEQ ID NO:20 or comprise a mutant sequence as described in the claims will produce a mutant sequence encoding a null mutant. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into

unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by McConnell et al (2001, Nature 411 (6838):709-713), who teach that the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain. This change renders the protein constitutively active and therefore creates a dominant mutation which has a drastic alteration in phenotype compared to wild-type *Arabidopsis* plants. In regards to the present invention, only mutations in specific amino acids cause a mutant phenotype in the PHABULOSA OR PHAVOLUTA proteins and not all mutations cause a mutant phenotype.

Hamada et al (1998, Plant Physiology 118:591-598) teach that expressing heterologous desaturases in plants does not always give predictable results. Hamada et al overexpressed a tobacco microsomal ω-3 fatty acid desaturase cDNA (NtFAD3) under the control of a mosaic constitutive promoter that confers about 10-fold higher levels of constitutive expression than the CaMV 35S promoter. The results of overexpression in tobacco plants resulted in a 40% increase

in alpha-linolenic acid in roots and only a 10% increase in leaves (abstract and page 593, right column, 1st paragraph of results). These results suggest that endogenous factors contribute to the observed result that cannot be predicted a priori.

Due to the unpredictable nature of plant transformation, one of skill in the art can not reasonably generate transformed plants with a desired phenotype using a specific isolated gene. Levels of transgene expression in plants are generally unpredictable and vary between independent transformants; this variability is usually explained by differences in transgene copy number and/or integration site (Finnegan and McElroy, 1994. Bio/technology 12: 883-888 pg. 883 2nd paragraph). In addition, Babiychuk et al (1997 Proc. Natl. Acad. Sci. 94:12722-12727) teach that homologous recombination in plants is very low (page 12722, left column) and that it is doubtful that homologous recombination will be practical in plants (page 12724, left column, 1st paragraph).

Given the claim breadth, unpredictability and lack of guidance as stated above; given the breadth of the claims which encompass a multitude of sequences that have not been exemplified; it would require undue experimentation by one skilled in the art to identify and isolate a multitude of non-exemplified mutant sterol C-5 desaturase nucleic acid encoding sequences from a multitude of non-exemplified plants, and to evaluate the ability of these sequences or variants thereof to cause the claimed effects in plants transformed therewith.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 65 and 73 and all subsequent dependent claims are directed to non-statutory subject matter. This rejection is made because the claims are drawn to "a delta-7 sterol C-5 desaturase coding sequence" and "A mutant delta-7 sterol C-5 desaturase" which does not indicate that the "hand of man" was involved in the invention. Amending the claim to recite "isolated" will obviate the rejection.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 57-62, 64-70, 72-75, and 77 are rejected under 35 U.S.C. 102(b) as being anticipated by Gachotte et al (1996, The Plant Journal 9(3):391-398).

The claims are broadly drawn to an isolated nucleic acid, or coding sequence that encodes a mutant delta-7 sterol C-5 desaturase polypeptide wherein said mutant delta-7 sterol C-5 desaturase is truncated in the N-terminal region of the polypeptide, N-terminal to a histidine cluster domain, or wherein the truncation occurs at a position N-terminal to the His1 or His3 histidine cluster domains, or wherein the truncation occurs at a position C-terminal to the His2 and N-terminal to the His3 histidine cluster domain, or wherein the isolated nucleic acid comprises a polynucleotide consisting of positions 143 to 322 or 143 to 1552 of SEQ ID NO:20 or a polynucleotide having 70% identity to one of the previous two sequences, and host cell.

Gachotte et al teach a nucleic acid sequence exhibiting 99.1% sequence identity to bases 143 to 322 of SEQ ID NO:20 transformed into yeast. It would be inherent that a plant

expressing said mutant delta-7 sterol C-5 desaturase would exhibit an approximate four-fold increase in episterol compared to a corresponding plant not expressing said desaturase, and as such, Gachotte et al anticipate the claimed invention.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 57-62, 64-70, 72-75, and 77 are rejected under 35 U.S.C. 102(a) as being anticipated by Choe et al (1999, The Plant Cell 11(2):207-221).

The claims are broadly drawn to an isolated nucleic acid, or coding sequence that encodes a mutant delta-7 sterol C-5 desaturase polypeptide wherein said mutant delta-7 sterol C-5 desaturase is truncated in the N-terminal region of the polypeptide, N-terminal to a histidine cluster domain, or wherein the truncation occurs at a position N-terminal to the His1 or His3 histidine cluster domains, or wherein the truncation occurs at a position C-terminal to the His2 and N-terminal to the His3 histidine cluster domain, or wherein the isolated nucleic acid comprises a polynucleotide consisting of positions 143 to 322 or 143 to 1552 of SEQ ID NO:20 or a polynucleotide having 70% identity to one of the previous two sequences, and host cell.

Choe et al teach a nucleic acid sequence exhibiting 100% sequence identity to bases 143 to 1552 of SEQ ID NO:20. For purposes of molecular biology, the sequence would be in a vector, operably linked to a transcriptional control element and transformed into a host cell. It would be inherent that a plant expressing said mutant delta-7 sterol C-5 desaturase would exhibit an approximate four-fold increase in episterol compared to a corresponding plant not expressing said desaturase, and as such, Choe et al anticipate the claimed invention.

9. Claims 61, and 69 are rejected under 35 U.S.C. 102(b) as being anticipated by Boudet et al (September, 1995 U.S. Patent Number 5,451,514.

The claims are drawn to a sequence which is a complement of any of the previous mentioned sequences listed in claims 61 and 69. The office interprets claims 61 and 69 to read on any sequence because Applicants have not specified a sequence that is "fully" complementary to the previous sequences. As written, a complement sequence can comprise one base pair.

Boudet et al teach a DNA sequence that shares at least one base pair with the mentioned sequences and as such, Boudet et al anticipate the claimed invention.

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist, who may be contacted at 308-0196.

Stuart F. Baum Ph.D.

July 1, 2003

ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1800